

Amendments to the Drawings

Figure 7 is newly added and provides the identical schematic which has been deleted from page 11 of the specification.

Attachment: New Sheet

REMARKS/ARGUMENTS

In response to the office action of May 16, 2008, Applicants have amended the specification and claims, which when considered with the following remarks is deemed to advance prosecution of this application. Favorable consideration of elected claims 6-10 and 16 is respectfully requested.

On page 2 of the office action, the Examiner has requested the specification be reviewed for sequences which are not part of the Sequence Listing, and both list and identify them with a proper sequence identifier in the Sequence Listing.

In response to the Examiner's request, the specification has been amended to add the Sequence Identifiers SEQ ID NOS: 9 and 10 to page 14 of the specification. The sequences corresponding to SEQ ID NOS: 9 and 10 have also been added to the paper and computer readable form (CRF) of the Sequence Listing submitted herewith.

In addition, paragraphs 1 through 4 of page 3 of the specification have been amended to indicate that sequence of Accession No. X04500 corresponds to SEQ ID No:11. The X04500 sequence, which was publicly available at the time the present applicaton was first filed, has been added to the Sequence Listing submitted herewith as SEQ ID No:11.

The specification has been objected to due an allegedly embedded hyperlink. By this amendment, the embedded hyperlink appearing on page 13, line 3, has been deleted. The specification has also been objected to for presenting a figure on page 11. By this amendment, the "Study Schematic" has been deleted from page 11 of the specification. The subject matter of the "Study Schematic" on page 11 is now submitted as an additional figure (Figure 7) and labeled in the top margin as "New Sheet."

Claims 8 and 10 have been objected to as referring to tables. By this amendment, claim 8 is canceled. Claim 9 has been amended to depend from claim 7. Claim 7 has been amended to recite the immunosuppressant medication listed in Table 2. Claim 10 has been amended to recite the cholesterol-lowering medication listed in Table 1. Withdrawal of the objection to claims 8-10 is respectfully requested.

Claims 6-10 and 16 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly directed to non-enabled subject matter. It is the position of the Examiner that since the claims refer to

GenBank Accession No. X04500, the claims incorporate by reference the subject matter of the sequence set forth in GenBank records. According to the Examiner, such an incorporation by reference is improper because the sequence is necessary to describe the claimed invention. By this amendment, the recitation of "X04500" in claims 6 and 7 has been replaced with "SEQ ID No.11." The sequence of Accession No. X04500 has been entered into the Sequence Listing as SEQ ID No.11. The sequence of Accession No. X04500 was publicly available at the time this application was first filed. No new matter has been introduced into the application. Withdrawal of the rejection of claims 6-10 and 16 under the enablement provision of 35 U.S.C. 112, first paragraph is therefore warranted.

Claims 6-10 and 16 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly directed to non-enabled subject matter. According to the Examiner, the specification does not provide enablement for determining the degrees of serum cholesterol elevation in "any" patient by the detection of "any" mutation in response to "any" immunosuppressant with "any" length of treatment.

In order to advance prosecution of this application, claims 6 and 7 have been amended to recite a human patient and a human IL-1 β gene, and the immunosuppressants rapamycin, everolimus, mycophenolic acid, mycophenolate mofetil, azathioprine, cyclosporine, and tacrolimus.

On page 10 of the office action, the Examiner has posited:

The specification teaches homozygous C at -31 is indicative of elevated cholesterol. The specification thus teaches patients with immunosuppressive who had the homozygous C at -31 were more likely to have higher cholesterol than those who did not. The specification does not teach the elevation is due to the immunosuppressive treatment, as the specification does not provide data for patients prior to treatment.

In response, Applicants respectfully submit that it had already been established that increased serum cholesterol levels during treatment with an immunosuppressant drug such as everolimus or with mycophenolic acid, is a serious side effects in patients. See specification, page 2, third full paragraph.

On page 12 of the office action, the Examiner has cited *Pediata Polska* (2004) volume 79, pp. 127-134, for teaching that the presence of the C(-31)T mutation did not result in altered

cholesterol synthesis in polish children. In response, Applicants respectfully submit that the reference did not examine the effect on cholesterol levels during treatment with an immunosuppressant drug selected from rapamycin, everolimus, mycophenolic acid, mycophenolate mofetil, azathioprine, cyclosporine, or tacrolimus.

Accordingly, withdrawal of the rejection of claims 6-10 and 16 under the enablement requirement of 35 U.S.C. 112, first paragraph, is respectfully requested.

Claims 6-10 and 16 have also been rejected under the written description provision of 35 U.S.C. 112, first paragraph. In response to the rejection, claims 6 and 7 have been amended to recite a human IL-1 β gene. Further, Accession Number X04500 has now been entered into the Sequence Listing as SEQ ID NO:11. Withdrawal of the rejection of claims 6-10 and 16 under the written description provision of 35 U.S.C. §112, first paragraph, is respectfully requested.

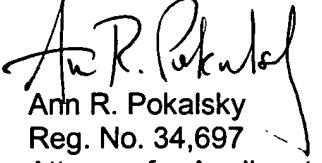
Claims 6-10 and 16 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for facility to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As discussed *supra*, the sequence of Accession No. X04500 was publicly available as of the filing date of this application. In response to the rejection, Applicants have entered the nucleotide sequence of Accession No. X04500 into the Sequence Listing as SEQ ID No.11. Claims 6 and 7 have been amended to recite “position 1903 of SEQ ID No. 11.” Claim 16 has been amended to recite “a chromosome” rather than “said chromosome.” Withdrawal of the rejection of claims 6-10 under 35 U.S.C. §112, second paragraph, is therefore respectfully requested.

Claim 16 has been rejected under 35 U.S.C. §102(b) as allegedly anticipated by El Omar (2000) *Nature* 404:398-402. As the Examiner has suggested, claim 16 has been amended to depend from claim 6 rather than claim 1. Withdrawal of the rejection of claim 16 under 35 U.S.C. §102(b) is therefore warranted.

In view of the foregoing remarks and amendments, it is firmly believed that the present

application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,


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